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ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE
DISEASES OF INFANTS AND CHILDREN
JOHN FITCH LANDON, M.D., Editor

LEADING ARTICLES IN THIS NUMBER

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1. Fox, C. L., Jr., et al.: An Electrolyte Solution Approximating Plasma Concentrations with Intravenous Potassium for Routine Use and Electrolyte Replacement, J. A. M. A., March 4, 1957.

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Wallace R. Roy, Ph.D., Director of Research

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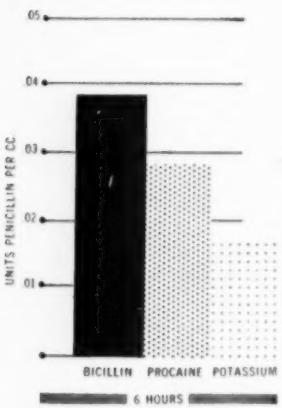

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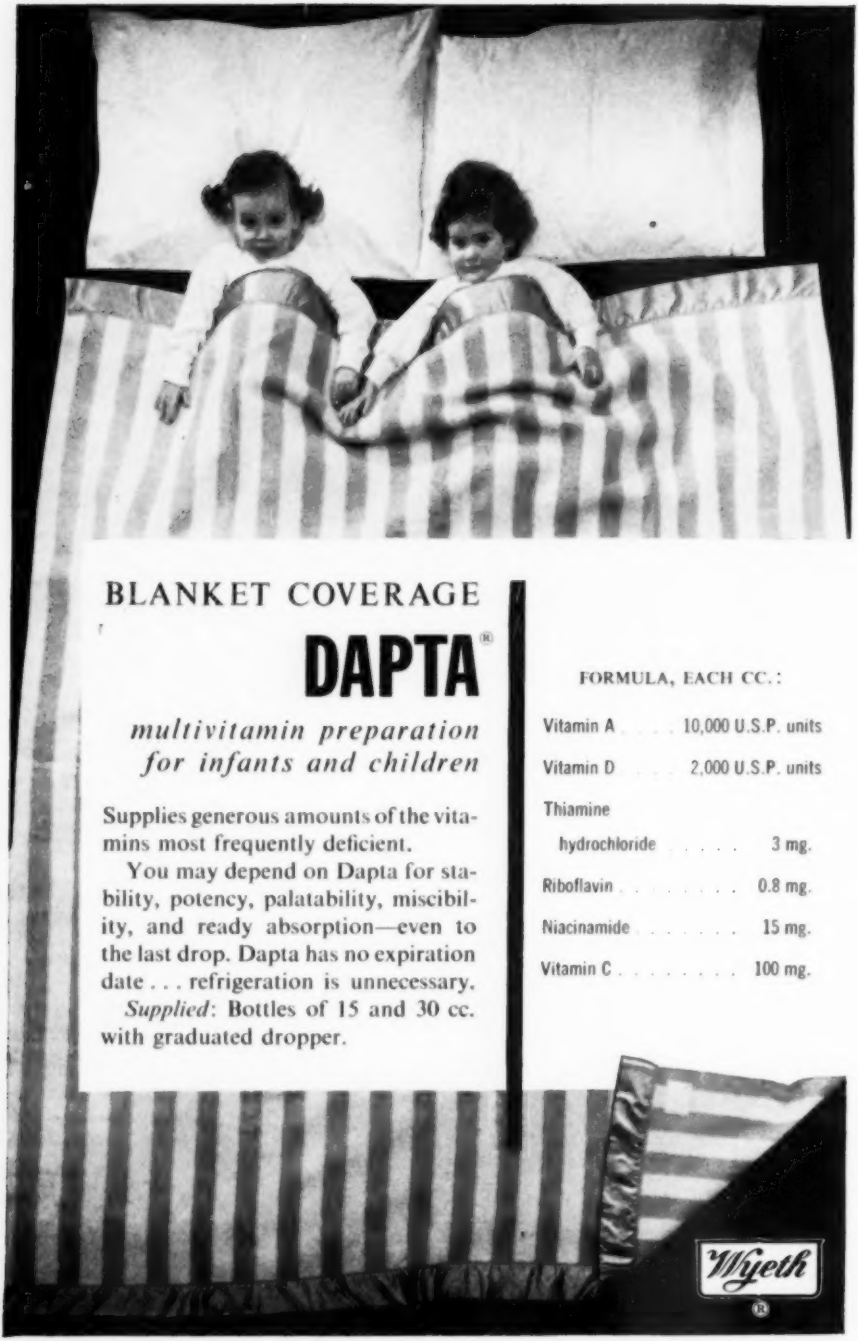
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ARCHIVES OF PEDIATRICS

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JOHN FITCH LANDON, M.D., Editor

NEPHROSIS COMPLICATED BY ACUTE PERITONITIS*

REPORT OF CASE

HARRY BLOCH, M.D.,
MARTIN JACOBS, M.D.,
AND
ANDREW BEDO, M.D.
Brooklyn

In 1930, Stewart[1] reported 21 deaths in 23 cases of pneumococcus peritonitis complicating nephrosis. In 1935, Schwarz and Kahn[2] recorded 15 deaths from peritonitis in 36 cases of nephrosis. They cultured a pneumococcus from the peritoneal fluid in ten, Streptococcus hemolyticus in two and Streptococcus viridans in one. Tappan[3], in the same year, published a study of 33 cases of nephrosis with seven deaths from pneumococcus peritonitis. She included a report of 50 cases from the literature with 18 deaths from pneumococcic and streptococcic peritonitis.

From 1942-1952, sixty-two children were admitted to the pediatric wards of the Kings County Hospital with the diagnosis of nephrosis complicated by acute bacterial infections. In no instance was peritonitis either a presenting complication or a development under treatment. All infections responded to antibiotic therapy. The recent admission of a child with nephrosis complicated by acute peritonitis offered an opportunity to observe the affect of antibiotics in both conditions and to survey our cases of

*From the Pediatric Service, Open Division, Kings County Hospital, Dr. L. S. Mullin, Director.

Prior to 1940, the literature of nephrosis was often concerned with the incidence of peritonitis, the mortality it entailed and the bacteria implicated.

nephrosis, since the advent of antibiotics, as to complicating infections encountered and bacteria involved.

CASE REPORT

A female white child, aged nine years, was admitted to the Kings County Hospital on February 2, 1952. The patient appeared acutely ill. There were marked pallor, rapid respirations and considerable swelling and edema of the face, extremities and body. The throat was intensely red. Over the left chest posteriorly and in the axilla, the breath sounds were absent and the percussion note flat. The abdomen was large, distended and extremely tender. The temperature was 103° F.

The mother stated that the onset occurred four days before admission with puffiness of the face and dark, scanty urine. This was followed two days later with a rising temperature and vomiting. The patient had two previous admissions. In June 1951, the child entered the hospital with an infection of the respiratory tract and generalized anasarca. She responded to antibiotics and corticotropin (ACTH). In December 1951, a similar episode occurred.

Laboratory findings on admission: Urine contained albumin (4 plus); the total serum protein was 3.8 per cent with 2 per cent globulin and 1.8 per cent albumin; cholesterol was 242 mg. per 100 cc.

Chest radiogram revealed an extensive fluid collection in the pleural space of the left side.

A growth of Staphylococcus aureus was obtained from the nasopharynx. Every six hours an intramuscular injection of 600,000 units of procaine penicillin G in aqueous suspension was given. A peritoneal tap was done 18 hours after admission. Purulent fluid was obtained, which, on direct smear, showed gram-positive cocci in short chains. Penicillin, 600,000 units, and streptomycin, one gram, was instilled into the peritoneal cavity. Terramycin, 500 mg., was given intravenously and continued orally every 6 hours. When the symptoms failed to subside in 48 hours, gantrisin was substituted for terramycin in doses of four grams stat. and one gram every four hours.

On the fifth day, the bacteriologist identified the organism as a Streptococcus faecalis strongly sensitive to chloramphenicol. All antibiotics were promptly discontinued and oral chloramphenicol in doses of 500 mg. stat. and 250 mg. every six hours was sub-

stituted. We then observed a series of interesting results. On the third day of therapy, the temperature became normal and the abdominal tenderness disappeared. By the seventh day, the child began to eliminate large quantities of urine. By the twelfth day, the patient's general appearance returned to normal. Physical examination of the chest now indicated almost complete absorption of fluid in the left pleural space.

The patient was discharged April 25, 1952 (59 days of hospitalization). The nephrosis was in complete chemical and clinical remission; the left lung was re-expanded; the abdomen soft and without palpable masses. To exclude the possibility of peritonitis

TABLE 1. *Infections Complicating Nephrosis*

Complication	No. of Cases
Pneumonia	13
Infection of the respiratory tract	12
Acute tonsillitis	11
Bronchitis	4
Otitis media	3
Measles	3
Mumps	2
Infection of the urinary tract	2
Infectious diarrhea	2
Appendicitis	1
Mesenteric adenitis	1
Pertussis	1
Encephalitis	1
Tracheitis	1
Sinusitis	1
Pleuritis	1
Conjunctivitis	1
Glossitis	1
Stomatitis	1
Peritonitis	1
Total	63

due to a ruptured appendix, a barium enema was given. A normal appendix was visualized.

DISCUSSION

In the past decade, 1942-1952, there were 29 children observed with the nephrotic syndrome. As shown in Table 1, there were 63 admissions with a complicating bacterial infection. Pneumonia, infections of the upper respiratory tract, bronchitis, otitis media and tonsillitis accounted for 43 or 68 per cent. The remaining 20 admissions were associated with measles, mumps, pertussis, infec-

tion of the urinary tract, infectious diarrhea, appendicitis, mesenteric adentis, encephalitis, sinusitis, pleuritis, conjunctivitis, tracheitis, glossitis, stomatitis and peritonitis.

Table 2, notes the microorganisms that were cultured from infections complicating the nephrotic condition. In many instances more than one organism was isolated. The pneumococcus was identified

TABLE 2. *Microorganisms Cultured From Complicating Infections*

Site	No. of Cultures	Organisms	Frequency
Throat	17	Pneumococcus	7
		Streptococcus hemolyticus	5
		Streptococcus viridans	5
		Streptococcus non-hemolyticus	5
		Staphylococcus aureus	5
		Staphylococcus hemolyticus	1
		Neisseria catarrhalis	4
		Diptheroids	2
		H. influenzae	1
		B. alkaligenes	1
Nose	10	Staphylococcus aureus	8
		Staphylococcus hemolyticus	3
		Streptococcus hemolyticus	2
		Micrococcus catarrhalis	1
Urine	7	Proteus vulargis	3
		B. coli	2
		Streptococcus non-hemolyticus	2
		Streptococcus hemolyticus	1
		Staphylococcus aureus	2
		Diptheroids	2
		Staphylococcus albus	1
		B. welchii	1
Blood	3	Staphylococcus aureus	1
Stool	1	Salmonella tennesseei	1
Eye	1	Staphylococcus aureus	1
Tongue	1	Staphylococcus aureus	1
Peritoneal cavity	1	Streptococcus faecalis	1

only seven times, whereas other bacteria were recognized 43 times in 27 cultures of the nose and throat.

MacLeod and Farr[4] observed that the organism cultured from the peritoneal fluid and the nasopharynx were frequently identical. In our patient, the peritonitis was caused by a Staphylococcus faecalis while a Staphylococcus aureus was isolated from the nasopharynx.

The excellent results obtained with antibiotics in peritonitis have been amply verified. Aldrich and Boyle[5], in 1938, had some success with erysipelas and scarlet fever convalescent serum. Schwarz and Weiner[6], in 1941, had good results with sulfapyridine. Palmer[7] used antipneumococcal serum in eight cases without success, but had had only one fatality in six cases treated with sulfapyridine. Levy[8], in 1947, noted a favorable response to intraperitoneal and intramuscular penicillin. In our case, administration of several antibiotics in adequate dosage was without result. Chloramphenicol, however, proved to be specific for the causative organism.

CONCLUSION

We have presented a case of nephrosis complicated by acute peritonitis. The organism cultured from the peritoneal exudate was a Streptococcus faecalis strongly sensitive to chloramphenicol.

A survey of 63 admissions of nephrotic patients with complicating bacterial infections showed the excellent response to antibiotics, the rarity of peritonitis as a complication and the infrequency of the pneumococcus as a cause of bacterial infections complicating nephrosis.

Acknowledgement is made to Dr. L. S. Mullin, director, and Drs. K. Jennings and A. Serri, attending pediatricians, for the privilege of using many cases from their services for this report.

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SOME UNUSUAL ACCIDENTS FOLLOWED BY MENTAL RETARDATION

WITH FOUR ILLUSTRATIVE CASES

HANS MAUTNER, M.D.
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Wrentham, Mass.

Mental retardation has a great variety of causes. We know the role of heredity in oligophrenia, and in many nervous or metabolic diseases. We have recently learned about the dangers of diseases of the pregnant mother to the unborn child. Animal experiments make it probable that also other conditions during pregnancy may become dangerous. Hormonal disturbances, asphyxia in any form, malnutrition, medication, intoxication, may play a role in these conditions which most commonly affect the brain. They are summarized by Francischatti and Bamatter and Bouguin[1] by the term embryopathy. Feeblemindedness may also result from occurrences which hit the child after birth. The consequences of encephalitis are well-known. The importance of accidents for the mental deterioration of children is often underestimated.

Therapeutic results in feeblemindedness have not been very promising. A damaged brain cannot be restored to normal activity. But this new approach to the etiology of some cases of mental retardation as a more or less accidental damage to the child before or after birth gives hope for a successful development of prophylactic measures as a means to depress the terrifying amount of feeblemindedness in the population.

Accidents are a source of mental retardation which could easily be avoided. Boldt[2] has recently stressed the high amount of accidents in the history of our feebleminded patients. We have at Wrentham State School at least 20 patients who are victims of severe accidents. Adding to this figure of approximately 1 per cent the birth injuries (12 per cent) we reach quite an appalling amount of mechanical brain injuries with consequent mental retardation.

I would like to demonstrate the role of accidents on some of our patients. We have accidents (1) before birth (attempted abortion); (2) at birth (birth injuries) and (3) after birth.

1. Abortion as a cause of feeblemindedness is probably not very rare, but rarely provable. We[3] have published two cases in which

drugs were taken for the purpose of abortion. Mechanical interference is most effective in producing abortion; attempted abortion with the sequel of the birth of a feebleminded child is seldom diagnosed. We will describe one such case.

2. Birth injury is generally accepted as a cause of feeblemindedness. The role of birth injury has been debated, but we have at least 12 per cent of our patients with this etiology. We know that prophylaxis here is very important. Development of obstetrical methods, education of physicians and nurses, and increasing understanding of the population with the following decrease of home deliveries has probably reduced danger. But there is one habit of great danger which is not stressed enough. We often hear that the attending nurse prevented delivery because the physician has not arrived. We have to stress this point of danger so that every nurse knows that this is not a medical procedure but a method to produce extremely severe damage to the brain of the child. We have at least six children under observation who are the victims of this easily avoided and dangerous procedure. We present one of the cases of our observation.

3. Postnatal accidents are also often avoidable. We give a car accident and a case of severe asphyxia to show one common and one very unusual type of accident.

ILLUSTRATIVE CASES

Case 1. Marie S., born October 5, 1943, the second child of intelligent parents. The first child and a younger child are normal. At time of pregnancy the mother worried because the father was overseas in the war. Two years after Marie's birth the mother had a miscarriage. Marie was born at full term, an easy delivery. At two years of age nystagmus was observed. She never talked or walked. She was examined in December 1944 at the Children's Hospital in Boston and the diagnosis of congenital cerebral defect, but definitely no subdural hematoma, was made. She was admitted to the Wrentham State School, a hopeless idiot with an I.Q. of .07. The head circumference was 52½ cm. The skull was irregular with a flatness on the left side of the occiput. The x-ray picture showed the skull increased in height with deepening of the posterior fossa and increase of the convolutional markings consistent with increased intracranial pressure. The lumbar spine showed a defect in the vertebral arch of L-1.

The child was a feeding problem, vomited very often, gained weight very slowly and died on December 27, 1951. Autopsy performed by Dr. Philipp Schwartz, revealed the following: the convolutions are rather narrow and thinner than normally. This is more marked on the left frontal lobe than on the right. The whole ventricular system is dilated to some degree. The aqueduct is mildly dilated, the fourth ventricle enlarged. The most extreme dilatation is seen in the upper part of the central canal of the spinal cord bordering the medulla. The floor of the dilated part is formed by a membrane which seems to be a scar. An approximately 2 cm. long, ½ cm. broad fissure corresponds to this part on the lower side of the medulla, caused by the separation of the pyramidal tracts. The aforementioned membrane separates two fissures: the lower is the sequel of the separation of the pyramidal tracts, the upper, the sequel of the separation of the funiculi graciles. The abducentes are very thin, the right facialis very flat and decolorized. Central surface of pons is very flat. The lateral corpora geniculata are very thin. There is a severe defect on the skull. Both occipital bones are affected. On both sides a large part of the bone is missing. The defect is filled by soft tissue. (The pathological anatomy of the brain and the skull will be published in detail). The whole picture is explained only by a direct mechanical injury to the neck and occiput of the fetus, probably an attempted abortion.

Case 2. Phyllis G., born September 11, 1944, the third child of very intelligent parents. The two older children are somatically and mentally well-developed. At time of birth the physician was not available and the attending nurse was very anxious to postpone delivery. She finally had to sit on the legs of the mother who was kept under light ether anesthesia for nearly one hour. After arrival of the physician the child was quickly delivered without instruments. She was lifeless, and it took a long period of artificial respiration until breathing set in. She was called a definite birth injury. Two and one-half months later she was seen at the Children's Hospital in Buffalo, N. Y. where blood was obtained by ventricular and spinal tapping. At four months of age, she had the first epileptic seizure and was seen at the Children's Hospital in Boston. There the spinal fluid was of normal color, the ventriculogram showed enlarged ventricles. Epileptic seizures were

observed all her life at long intervals. She was admitted to the Wrentham State School on January 22, 1947. Her I.Q. at that time was .39. She could not talk, had an alternating strabismus. At the Wrentham State School she learned to talk. She always was described as destructive. Epilepsy was controlled by means of dilantin and mebaral. In October 1950 she started to cough, showed dullness on the right side of the chest, a lung abscess developed and she had mild hemoptosis twice. The pulmonary disease was treated by means of aureomycin and seemed to react promisingly. But in April 1951 she had a severe epileptic fit and died within 15 minutes. The autopsy performed by Dr. Philipp Schwartz revealed the huge lung abscess and very severe pathology of the brain. The cortex, basal ganglia and medullary parts of the brain were affected. There was extended sclerotic shrinking of both occipital lobes; marked scarring and hardening of the cerebral gyri, especially in the lateral surface of both occipital lobes. Large defects of the caudate nuclei. Status marmoratus.

Case 3. Miriam G., born September 28, 1920, the daughter of highly intelligent parents. Normal delivery, normal development during the first month of life. At the age of six months a cat was found sitting on her face, the child severely cyanotic, unconscious; the attending physician had to apply prolonged artificial respiration before she started to breath again. From this time on she was spastic, never learned to walk or to talk. She was admitted to Wrentham on April 11, 1945. Her I.Q. was .03, a helpless idiot with spastic quadriplegia, exaggerated reflexes.

Case 4. Kathleen G., born October 3, 1946, was admitted to Wrentham State School on July 20, 1951. The parents are intelligent. Two younger brothers are developing normally. She was born full term, easy delivery, normal development at first. At 2½ months she was involved in a very severe car accident in which she fell out of the car and was hit on her head by the hub cap of the second involved car. She suffered a severe fracture of the skull and was treated for three weeks at the Sick Children's Hospital in Toronto. She was discharged with the mental diagnosis, idiot. At six months she had convulsions which were controlled by dilantin. She was seen in 1947 at the Children's Hospital in Boston where she was diagnosed as blind with optic atrophy. In 1947 she was operated at the Boston City Hospital

where a piece of bone was removed and a plate inserted which had to be removed again one month later. From this time on she seemed to improve, started to see and to say some words, etc., but the psychological examination does not show any improvement in her mental age. She has a bone defect of the occiput two inches in diameter. She sees and hears, is overactive but does not respond to her surroundings, does not speak, but has developed somatically very well. Her psychological test, however, gives her a mental age of 7 months, and an I.Q. of 12.

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FAMILIAL INCIDENCE OF MULTIPLE SCLEROSIS. (Brain, London, 74: 191, June 1951). Pratt and associates believe that the familial incidence of multiple sclerosis is greater than reports seem to indicate. They collected from the literature 184 families in which more than one case occurred and record an additional 33 families. In a series of 168 consecutive cases of multiple sclerosis seen by the authors over 18 months, there were 12 instances of one or more relatives being similarly affected. In an earlier series of 142 patients, in which the inquiry was more limited, there was a family history of the disease on eight occasions. Therefore, in a total of 310 cases the familial incidence was 6.5%. The case histories of affected members of families are recorded. The incidence of multiple sclerosis in the sibs of 168 persons with the disease and in the parents of 310 diseased persons is shown to be significantly higher than that expected on the basis of a random distribution of the disease. Also described is the occurrence of the disease in a mother and four of her daughters and an instance of the disease occurring by direct transmission in three generations. The clinical features and relative frequency of certain familial degenerative disorders of the spinal cord and of multiple sclerosis are compared. The present study supports the view that a genetic factor is present in multiple sclerosis and that there is evidence for both a dominant and a recessive mode of inheritance.—*Journal A.M.A.*

CLINICAL REVIEW

In order to encourage the writing of clinical articles by recent graduates or senior medical students, the ARCHIVES *will publish monthly at least one such paper from the classes of Doctor Reuel A. Benson, New York Medical College, New York, and Doctor Philip Moen Stimson, Cornell Medical School, New York. Other interested medical schools are cordially invited to submit student papers for consideration.*

NEUROLOGICAL COMPLICATIONS FOLLOWING ANTIRABIES VACCINATION*

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Rabies has been known to mankind since antiquity. The earliest description which has come down to us is the one by Democritus, written in 500 B.C. Rabies is an acute infectious viral disease of the central nervous system which is ordinarily transmitted to man by the bite of a rabid dog or another rabid animal. Pasteur, in the years 1881-1884, first demonstrated the presence of the causative agent of rabies in the central nervous system of rabbits by serial passage. He was also the first to use a vaccine to protect man from this dreaded disease. However, as early as 1887, the first case of postrabies vaccination encephalitis was described[22].

Antirabies vaccine for human use is essentially a finely divided suspension of central nervous system tissue of rabbits which have been killed while in the terminal paralytic stage of rabies caused by the fixed virus[39]. Various modifications of this vaccine have been used. The type commonly in use in the United States is the Semple type of vaccine which consists of a rabbit brain suspension of phenolized, fixed virus[32].

INCIDENCE

Various figures have been reported for the incidence of neurological complications after antirabies vaccination. Remlinger reports 329 cases of treatment paralysis in a series of 1,164,264 patients vaccinated which gives an incidence of 1:3500[35]. Simon reports 100 cases in a series of 217,744 patients—an incidence of 1:2200[9], and Sellers reports 7 cases in 50,000—an incidence of 1:7000[39].

*Submitted as partial fulfillment of the requirements of the course in Senior Pediatrics at the New York Medical College, Flower and Fifth Avenue Hospitals, New York.

Greenwood reports an incidence of 1:5814 in a series of 1,290,758 patients[11].

A striking fact is that children—although about 50 per cent of all treatments are given to children—show neurological complications relatively rarely[30]. From the literature one gathers that the patients are most frequently between 20 and 40 years. It is also interesting that males seem to predominate 2:1[26], at least according to one small series. However, no conclusion can be drawn from this study, because the numbers involved are too small. One paper states that Europeans are affected more often than Orientals, and intellectuals more often than laborers; at the same time it is stated that patients subjected to physical or psychic strain during the period of vaccination are more likely to show neurological sequelae[6]. However, this again is hardly conclusive.

It is, however, commonly believed and accepted today that the type of vaccine influences the frequency of neurological complications. There is fairly universal agreement that the greatest number of complications are due to fresh virus[6, 14, 33, 34, 40]. Holt quotes an incidence of 1:2500 with live virus vaccine, and of 1:9000 with dead virus vaccine[14].

TABLE I.

Incidence of Paralytic Accidents After Rabies Vaccine (from McKendrick).

Attenuated virus (Pasteur)	1:3000
Diluted virus (Hogyes-Harris)	1:3000
Phenol treated virus (Semple)	1:9000
Ether treated virus (Alivisatos)	1:10,000
Heat treated virus	1:18,000[33]

Moreover, the more intensive the treatment, the more likely is it that reactions will occur[34]. One author states that neurological complications don't usually occur if less than 10 injections are given[39].

The incidence of fatalities from neurological complications following antirabies vaccination has been calculated to be about 25 per cent[32]. One small series of 32 cases shows a mortality as high as 40 per cent[26].

For the sake of comparison it should be pointed out that no authentic instance of recovery from rabies has yet been reported[13, 32]. In a series of 46,000 patients bitten by rabid dogs and treated by vaccination .4 per cent got the disease, whereas in unvaccinated

groups about 15-16 per cent contract rabies[32, 31]. The unvaccinated groups, however, are not control groups in the strict sense of the word. Nevertheless, the evidence is strongly in favor of vaccination.

CLINICAL FINDINGS

Before specific cases are discussed it is well to analyze the neurological sequelae of antirabies vaccination. The "incubation" period between vaccination and the onset of the symptoms is quoted as being 10-12 days[37], 10-13 days[41] or 11-15 days. Rosen states that "no matter what the illness, if it appeared 11 days after vaccination that illness is postvaccinal"[36].

The signs and symptoms of this disease are manifold. Table 2, compiled by Remlinger[25], is quoted here, as it is considered to be most reliable, because Remlinger was in a position to analyze a total of 243 cases; other authors did not have such extensive material at their disposal.

TABLE 2.

Severe paraplegia with bladder and rectum symptoms	68
Landry's ascending paralysis	39
Paresis of both lower extrem. and bladder retention	33
Unilateral facial nerve paralysis	31
Paresis of lower extremity with bladder symptoms	21
Paralysis of facial nerve, type not stated	22
Bilateral facial nerve paralysis	5
Paralysis of cranial nerves VII and III	4
Simple paresis of the bladder	9
Miscellaneous neuritis	11

However, beyond this purely numerical recording of the frequency of symptoms and signs, an attempt has also been made to classify the neurological complications following antirabic treatment. Several types of reaction have been described[9, 12, 26, 39]:

(1). Generalized urticarial rash which usually develops in patients previously sensitized to brain tissue. It responds to epinephrine.

(2). Delayed local reaction characterized by the signs of inflammation—heat, swelling, redness, induration, tenderness and itching. This reaction is the most common one.

(3). More severe constitutional reaction with headache, fever, malaise, nausea, vomiting and generalized lymphadenopathy. These are the cases that later, if treatment is continued, often show a

neurological syndrome. Headache, nausea and vomiting are usually the prodromata of a developing encephalomyelitis.

(4). Peripheral nerve paralysis. These cases usually recover.

(5). Dorsolumbar myelitis—usually occurring on the 12th to 14th day of treatment with fever, numbness and tingling of the extremities, sphincter disturbances and progressive paralysis of the lower extremities. Here recovery is the rule, but about 6 per cent of the patients do succumb[30].

(6). Paralysis of the Landry type. This has severe, systemic symptoms—nausea, vomiting, headaches, fever, incontinence of urine and paralysis of the lower extremities. The paralysis ascends to involve the bulbar nuclei, and death often ensues. There is a fatality of 30-50 per cent[9]. Some recover completely; some are left with some degree of paralysis.

(7). Cerebral type. Here we may have all the signs and symptoms of an encephalomyelitis with papilledema and bradycardia.

CASES FROM THE LITERATURE*

Twenty-seven cases reported in the literature were reviewed by the writer of this paper. Since these cases are reported by many different authors, and since varying points are stressed by them it is not possible to tabulate the cases. And although no definite conclusions can be reached from such a small series it may be of interest to point out the following findings: Of these 27 patients, 19 recovered, whereas 8 died (mortality of 29.6 per cent). Males predominate at a ratio of 5:1. Children are comparatively rarely affected. Several of these patients had received a previous course of antirabic vaccination. The clinical signs and symptoms included all those reported in Table 2, and ranged from signs of isolated peripheral nerve involvement to signs of severe encephalomyelitis and ascending paralysis of the Landry type. Deaths were recorded in patients with a Landry type of paralysis, and in patients with encephalomyelitis. In those who recovered, recovery was usually complete except for occasional residual foot-drop[33], residual muscle atrophy[28] or muscle weakness.

CASE OBSERVED AT METROPOLITAN HOSPITAL

A.M.A., four-year-old, white, female, was admitted on June 20,

*1, 5, 9, 10, 12, 21, 26, 28, 30, 33, 34, 37, 40.

1951, with a chief complaint of lethargy and irritability of three days' duration.

Present Illness: On May 20, 1951 the child had been bitten in the left ankle by a dog. The wound was cauterized at St. John's Long Island City Hospital within one-half hour after the bite had been inflicted. No TAT was given. Since the dog could not be found, antirabies vaccination was advised and started at the Department of Health Station on June 5, 1951. Five injections were given (June 5, 6, 8, 9, 10), but one arm became swollen, and the child ran a temperature. So the Health Department suggested discontinuing the treatment. The last injection was given on June 10, 1951. On June 17, 1951 the mother noted lethargy and irritability, slight fever and marked anorexia, and a whining, wailing cry. The morning before admission the child was unstable when standing, and the mother noted twitchings of the left arm.

Past History: The child was born by normal delivery, had measles at the age of three years, scarlet fever at the age of four, in April 1951. There is also a history of frequent colds.

Family History: Not obtained.

Physical Examination: On admission the patient was drowsy and irritable, but could be aroused easily. Temperature was 99.4° F. Pulse rate 124 per minute, blood pressure 80/30, weight 34 pounds. The only noteworthy physical findings were those obtained by examination of the nervous system. The knee jerks were hyperactive bilaterally, and the Babinskis were questionably positive bilaterally. The extremities were spastic. There was no nuchal rigidity, Kernig and Brudzinski were negative.

Laboratory Examination: A *spinal tap* was done and clear fluid was obtained; there was no increase in pressure, Pandy was 1+, protein was increased and 4 cells were seen on microscopic examtion. Sugar and chlorides were normal.

Blood: RBC 4.2 million, WBC 10,650; polymorphonuclear 68, lymphocytes 30, eos. 2.

Treatment: The day after admission (June 21, 1951) the patient was started on penicillin and aureomycin, both of which were discontinued after two days. Phenobarbital was also given, and it was discontinued after five days.

Course: During the day of admission and during the following two days the general condition was much the same; the tempera-

ture fluctuated between 99° and 102° F. Fluids by infusion were given. Spasm in the arms increased and they were clenched in flexion. The patient developed bilateral foot-drop the day after admission. During a neurological consultation on that day generalized spasm of the muscles of the extremities was found, which spasm was most marked in the upper extremities and more marked in the right lower than the left lower extremity. No reflexes were present in the upper extremities and the abdominal reflexes were also absent. Deep tendon reflexes in the lower extremities were active with some preponderance of the left. There was fanning of the toes bilaterally, more marked on the left. Babinskis and Gordons, sensory disturbances, cranial nerve involvement, nuchal rigidity and fundal changes were absent. Fine clonic movements of the hands, occurring in spells, were noted.

On the same day a blood pressure of 170/130 in the left and 150/120 in the right arm was noted. It returned to normal the following day and has remained so ever since, systolic pressure ranging from 105-118mm., diastolic from 60-70mm. After the third hospital day a gradual deterioration set in, the patient becoming increasingly lethargic and drowsy, although there were intervals during which the child was alert and in contact with her surroundings. Marked flexor spasm of the upper extremities was noted, and marked spasm also in the lower extremities, especially on the left. Occasional twitching of the muscles of the arm, face and tongue was observed. The weight in one week fell from 34 to 31 pounds.

On the tenth hospital day (June 30, 1951), generalized clonic convulsions lasting several minutes were observed; sporadic clonic movements of the right upper extremity were also noted. The temperature rose as high as 107°., the heart rate was 170 per minute, pulse rate 140 per minute. Since diminished breath sounds were heard over the right lung fields anteriorly, intensive antibiotic treatment was started; penicillin and streptomycin were given. In addition phenobarbital was again given, and rubramin was started. It was necessary to have recourse to tube feedings because the patitent was unable to swallow.

Following this episode the condition remained poor, and a repeat neurological consultation on the fourteenth hospital day (July 4,

1951) brought the neurologist's opinion that the prognosis was poorer than before. The patient was less alert, reacted sluggishly to painful stimuli. Respirations were lightly auxiliary. There was slight rigidity of the neck and spastic paralysis of both hands and both legs, more marked on the left. Fanning of the toes was present on the right, a definite Babinski on the left. Knee jerks and ankle jerks were hyperactive with a predominance of the left. Some twitches of the upper and lower lip were noted.

On the seventeenth hospital day (July 7, 1951) a blood transfusion (500 cc. of banked blood) was given. Two days later the patient again started to have some lucid intervals, and would occasionally respond to talking. Deep tendon reflexes were markedly hyperactive.

The temperature returned to a lower level on July 17, 1951, and the patient started to show a gradual weight gain. The sensorium remained unchanged with frequent lucid intervals during which the child seemed alert, the gaze of the eyes was clear, alternating, however, with periods of apparent drowsiness during which the patient was out of contact and uttered shrill cries. The spasm also decreased gradually, and tremors were observed less frequently. The knee jerks remained hyperactive. The general condition was one of weakness, but the child was able to move both legs and arms. By July 18, 1951 the patient was also able to swallow some fluids, so that oral feedings could be administered between gastric feedings, and gradual general improvement continued. Otherwise the course was uneventful except for a bout of diarrhea lasting for two days from July 16 to July 18, 1951. There were never any marked respiratory difficulties at any time throughout the course of the illness. As soon as any signs of improvement were observed the child was placed under the care of the Physiotherapy Department.

On July 23, 1951 the patient was able to swallow solid foods; she recognized people, smiled and was able to obey suggestions, such as to shake hands, scratch her nose, etc. She was also able to sit without support for a short time and could move all extremities. By the end of July all deformities had largely disappeared, there was a good range of motion in all joints, and the sensorium was clear.

Further recovery was uneventful, and the child was discharged on September 4, 1951 with a diagnosis of encephalitis due to rabies vaccine.

A summary of medication and treatment, and of laboratory findings follow:

Medication and Treatment: The child was placed in bed. A foot-board was provided to prevent contracture of the gastrocnemius muscles. A board for the spastic left hand was provided but later discontinued on advice of the Physiotherapy Department. During the acute phase a special fluid diet of oz. 8 q4h was given which provided about 1700 calories per day. Water (about 5 oz.) was given between the feedings, providing a total of 1600 cc. of fluid. Later a regular diet was provided. Vitamin preparations were administered throughout, Vi Synerol at first, later Vi Penta gutta XV b.i.d.

Medication:

1.	Penicillin 100,000 U. q3h	6/21 – 6/23; 7/1 – 7/13
2.	Aureomycin 250mg. q4h	6/21 – 6/23
3.	Streptomycin 500mg. b.i.d.	6/30 – 7/13
4.	Aspirin gr. iv q4h p.r.n.	6/30 – 7/ 1
	gr. v OD	7/ 1 – 7/ 7
5.	Phenobarbital gr. ½ q6h	6/21 – 6/25
	gr. ⅜ q6h	6/30 – 7/ 1
	gr. ¼ q6h	7/ 1 – 7/13
6.	Rubramin 15 microgram b.i.d.	6/28 – 8/11
7.	Transfusion—500 cc. blood	7/ 7
8.	Physiotherapy started	7/17

Laboratory Reports:

Spinal Fluids

Date	Cells	Sugar	Protein	Chlorides	Culture
6/20/51	4	66mg%	60mg%	740mg%	
6/26	90, predom. L	57mg%	95mg%	595mg%	negative
7/ 3	200 " "	62mg%	45mg%	685mg%	negative
7/14	95 " "	52mg%	64mg%	700mg%	
8/11		56mg%	21mg%	718mg%	

Wassermann—6/20—negative serum.

Blood

Date	Hgb	RBC	WBC	P	L	E	M	Culture
6/20		4.2 million	10,650	68	30	2	..	
6/22								negative
6/28	9gm	4.3 million	13,200	60	32	4	4	
6/30		3.2 million	13,500	84	14	..	2	Staph. albus
7/ 6	10.5gm							
7/16	11gm	4.4 million	10,000	62	36	1	1	
7/18								Staph. albus, coagulase neg.

Urine Analysis

Date	RBC	WBC	Casts	Protein	Sugar	Acetone	Culture
6/21							negative

6/22	none	rare	none	none	none	none	negative
6/23	many	many	occas.	none	none	none	
6/29	occas.	many	occas.	1+	none	none	
	Also not catherterized.						
7/18							hemol. strept.

Blood Chemistries

Date	FBS	BUN
6/22	91mg%	14mg%
6/25	103mg%	9.5mg%

Chest x-rays—6/28 and 8/23 within normal limits.

E.C.G.: 8/13/51—within normal limits for a child 4 years of age.

Serological Tests for Virus and Rickettsial Diseases were carried out at the Bureau of Laboratories, Department of Health, City of New York on specimens taken on June 28 and July 17. Tests were negative on both occasions for lymphocytic choriomeningitis, eastern equine encephalitis, western equine encephalitis, St. Louis encephalitis, Japanese type B. encephalitis and mumps.

Revised Stanford-Binet Intelligence Test was carried out on August 27. The I.Q. was 94. The impression was that this is a child who tests in the average range. There are no indications of brain injury. She appears emotionally stable and well adjusted.

PATHOLOGY

The pathology involves both gray and white matter[4]. Demyelination is perhaps the most outstanding pathoiogical feature in neuroparalytic accidents following the administration of antirabic vaccine[22]. Demyelination, however, can be produced by a variety of agents, and is believed to be merely a response of the white matter of the central nervous system to injury—which response need not necessarily be fatal to the tissues[16].

Gross Pathology: When the meninges are involved, which may or may not be the case, they are found to be edematous and hyperemic. Occasionally there is an exudate over the pia[9]. The central nervous system is grayish-pink in color, shows edema and softening, and may show petechial hemorrhages[9]. Although lesions may be found anywhere, the dorsolumbar region of the spinal cord is involved most frequently; the medulla is affected more frequently than the encephalon[9].

Microscopic Examination reveals a varying degree of perivascular softening and atrophy of the central nervous system, especially

around small venules and arterioles[4]. There are perivascular foci of lymphocytic infiltration, and occasionally collections of plasma cells, granular corpuscles[9] and red blood cells[26]. The blood vessels so affected, however, are not occluded[4], but may also be surrounded by small hemorrhagic areas with demyelination and proliferation of oligodendroglia[9, 26]. Practically all reports agree that there are no Negri bodies to be found[30].

The Cerebrospinal Fluid is not typical[30]. Pressure may be normal or increased. The proteins are generally increased; albuminocytologic dissociation has been found by some[28, 29]. Sugar and chlorides are not typical. The number of cells per cubic millimeter ranges from normal to such values as 1,181 W.B.C. per cubic millimeter with 98 per cent polymorphonuclear neutrophils and 629 R.B.C. per cubic millimeter[26], or 800 W.B.C. with 90 per cent polymorphs[9] or 120 W.B.C. with a predominance of lymphocytes[5].

ETIOLOGY

Various theories concerning the etiology of neuroparalytic accidents following antirabic vaccination have been advanced over a period of many years. It was at first thought that the reaction was due to the street virus of rabies, and that the disease was a modified form of rabies. Another theory postulated that it was due to the fixed virus[9]. Still others believed that while the virus of rabies was not responsible, the neuroparalytic accident was due to the activation of a latent virus in the host's central nervous system[2] or, simply, that an unknown virus caused it[4].

Some authors believed that signs and symptoms to be due to a neurotropic virus normally present in rabbit spinal cord[9]. However, not all authors believed that a virus was the cause. Allergy was suggested by Horack[15], because he found that individuals with a personal or family history of allergy are more prone to develop complications following vaccination[37] and that revaccination has not only the effect of a booster dose[27], but that complications are more likely to develop in patients who have been previously vaccinated against rabies[39]. Lastly, isoimmunization to brain tissue was suggested as an etiologic factor[9, 20, 26].

EXPERIMENTAL WORK

Experimental work has been done to prove or disprove these theories, especially the last two of allergy and isoimmunization to

brain tissue. An attempt was made to produce neurological symptoms in guinea pigs, rats and mice by means of a single injection of various organ emulsions. When homologous and heterologous brain tissue was injected, neurological disturbances occurred, characterized chiefly by paralysis of the hind limbs[23]. Schwentker and Rivers induced a complement fixing antibody in rabbits by injection of aqueous suspension and alcoholic extract of rabbit brain. They concluded that there was organ specificity, but no species specificity[38]. Neurological manifestations were also found in 4 out of 60 Great Pyrenees when antirabies vaccination was given. However, no antibrain antibody could be demonstrated in the sera of these dogs[17].

The most important experiments were those done with monkeys. Kabat and his co-workers injected homologous and heterologous brain tissue into Rhesus monkeys, using Freund's adjuvant technique. Symptoms noted in the monkeys were ataxia, quadriplegia, strabismus, ptosis, hemiparesis, weakness of all, several or one extremities, twitching nystagmus, facial weakness, blindness, tremors and auditory hypersensitivity. The pathology consisted mostly of small, inconspicuous lesions, the foci being perivascular in distribution. The white matter was primarily involved with less intense, independent changes in the gray matter. The lesions were mostly in the brain, and only rarely in the spinal cord. Microscopic examination of the early stages showed polymorphonuclear neutrophils, congestion and perivascular demyelination; later the neutrophils were replaced by lymphocytes and large mononuclear cells; still later microglial proliferation set in. Kabat and his co-workers concluded that the experimentally produced disease involved the formation of antibody to the injected brain which reacted with the antigen in the central nervous system of the animal to produce the disease[18].

Morgan, also using Freund's adjuvant technique, injected homologous central nervous system tissue into monkeys, and found clinical symptoms rather similar to those observed in humans setting in on an average of 2½-5 weeks after injection. The reactions were mostly to white matter, so that the conclusion was reached that gray matter is not—or only slightly—antigenic[21]. The pathology and distribution of the lesions were similar to that found by Kabat et al.[18].

Ferraro, in 1940, injected rabbit brain into monkeys intramuscu-

larly and got signs of central nervous system involvement which was progressive[8]. In 1944, Ferraro performed further experiments and found the pathological changes in the brain similar to those in human beings. He concluded that there is a symptomatic inflammation—a local reaction to disintegrated material[7]. It appears that the chemical fraction of brain tissue which serves as an organ specific hapten in the production of demyelination is lipoidal in nature[42]. Others, however, have postulated a complex polysaccharide[3].

Although this evidence is very suggestive, there are some points that merit consideration. Despite the similarity between the experimental and clinical lesions there are also some differences. The inflammation in the monkeys is usually far beyond that observed in human beings. In the monkeys there is a paucity of lesions in the spinal cord[18]. And while a special reaction of the animal brain may explain these differences, the same possibility of a special, different reaction of the animal brain may suggest similarities where none exist[43]. In addition, it is well to be aware of the fact that practically every vaccine, serum or other biological has at some time or other caused neurological symptoms similar to those following rabies vaccine[30]. Also, prior to better methods of control of epilepsy, injections of brain emulsions were given to reduce the frequency of seizures. Stavrovskaja treated 60 patients with one cc. doses every day for 3 years without complications[41]; other similar treatments are reported—also without the neurological sequelae observed sometimes after antirabies vaccination[19].

Another series of experiments has attempted to prove the presence and evaluate the significance of complement fixing antibodies against brain tissue in the sera of individuals who had received antirabies vaccine treatment. Koprowski et al. found that the complement fixing antibody was obtained only in individuals who had received more than 7 days of treatment. Titers were determined in 3 patients who developed neurological complications, and were found very high in 2 cases, but low in the third case[24]. Le Bell et al. also found that revaccination had a booster effect[27]. Kirk and his co-workers found that the complement fixation test becomes positive between the 15th and 18th day. A very high titer—and an earlier rise in titer, was found in a patient who developed neurological sequelae[20].

PREVENTION AND TREATMENT

Since the etiology, despite all the experiments, is not entirely clear we have no absolute way of preventing neurologic complications following antirabies vaccination. There are, however, a few suggestions which seem worth while to follow. Exertion should be avoided while vaccination is being given[27], and so should alcohol[1, 21]. While we have no proof that these two factors really influence the development of neurological complications, it seems reasonable to follow these suggestions which must be—if nothing better—at least completely innocuous. Horack suggests desensitization in cases that show a marked local reaction following subcutaneous injection of a small test dose. He believes that graduated doses should be given until a full dose can be used without producing marked local effects. Desensitization should be carried out both at the beginning of the treatment and whenever a marked local reaction develops during treatment[15].

Koprowski et al. report that the use of one injection of hyperimmune antirabic serum concentrate protected hamsters and guinea pigs against rabies, and that the additional use of rabies vaccination neither enhanced nor diminished the value of this treatment. A small number of humans were also treated with uniformly good results, but the series was too small for a final conclusion[25].

No specific treatment for these neurological complications is available at this time. General supportive measures, including antibiotics and chemotherapy for the prevention of infection, are most important. Phsyiotherapy has to follow in time to assure a maximum return of function and optimal functional results. Vitamin B preparations are commonly used on an empirical basis. Antihistaminics have been used a few times, sometimes with apparently good results, and without results at other times[12]. Cortisone has been used on one case reported in the literature, and the authors claim excellent results. They base this treatment on experimental work done by Kabat and others who found that the development of those lesions is blocked by ACTH in experimental animals[10].

COMMENTS

Obviously, antirabies vaccination is not an entirely harmless procedure. Nevertheless, in view of the hopeless prognosis of

rabies, and in view of the incidence of neurological complications following vaccination, it would be irresponsible to condemn antirabies vaccination and to discontinue it. If the animal reservoir could be controlled or eliminated the necessity for vaccination and the complications thereof would decrease considerably; but that is beyond the scope of this paper. As was pointed out above, we do not know the etiology of the neurological complications. While the experiment with hyperimmune antirabic serum sounds very promising, and while in its perfection and ultimate use may lie the answer to our problem, further research will have to be done and the outcome awaited before any definite statement about the value of this kind of treatment can be made.

This leaves us to attempt an accurate definition of the indications and advisability of using antirabies vaccine. The writer believes the following to be absolute indications for vaccination:

1. A bite, especially on the face, hands or arms by an animal proven clinically or by laboratory tests to be rabid, or by an animal suspected to be rabid.

2. A bite by a stray animal in an endemic area.

3. The contamination of fresh abrasions by the saliva of a rabid animal.

To minimize neurological complications the following precautions are suggested:

1. The person receiving vaccination should be skin-tested and desensitized by the method described by Horack, if necessary.

2. An individual who has received antirabies vaccination before should be given only a short booster series of injections—a total of 5-6 injections. Such an individual should be watched very closely throughout and for 2 weeks following the course of treatment.

3. Any individual who shows systemic involvement during a course of treatment should receive no further injections.

Animal experiments will have to be continued to furnish absolute proof of etiology. Further tests with titers and a simple method for determining titers might be of value in that an early, marked rise in titer could then also serve as an indication for discontinuation of treatment. The value of ACTH, cortisone and antihistaminics in actual treatment will also have to be subjected to further investigation.

SUMMARY

1. The incidence, pathology, theories regarding the etiology, and the clinical signs and symptoms of neurological complications following antirabies vaccination are discussed.

2. A case observed during the summer of 1951 at Metropolitan Hospital is presented.

3. Experimental work relating to this disease is mentioned and briefly discussed.

4. Measures for the prevention and treatment of neurological complications are reviewed and evaluated. Indications for antirabies vaccination are proposed, and special precautions to be observed during the course of vaccination are mentioned.

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Wherever in the bibliography, an author is referred to with the term "as quoted by" the original reference was not available at the libraries of the New York Medical College, the New York Academy of Medicine, or Metropolitan Hospital.

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AGE OF CHILDREN AT OPERATION FOR HARELIP AND CLEFT PALATE. (Philippine Medical Association Journal, Manila, 28: 20, Jan. 1952). Operations for both cleft lip and palate should always be completed before the child reaches the age of two years. Children with both harelip and cleft palate should be operated on in two stages. In such children Laico repairs the harelip first, when the child is about two months old, and the cleft palate when the child is 18 months old. In cases of harelip without cleft palate, whether unilateral or bilateral, the operation is best performed as early as the age of five months. Operations for cleft palate alone should be done as early as 18 months. In cases of bilateral harelip with cleft palate, the author operates on the harelip first on one side at the age of 2 months. When the child is strong enough, he repairs the other side of the upper lip. Then when the child is 18 months old, he operates on the cleft palate.—*Journal A.M.A.*

DEPARTMENT OF ABSTRACTS

WILSON, J. W.; LEVITT, H.; HARRIS, T. L. AND HEILIGMAN, E. M.: TOXIC ENCEPHALOPATHY OCCURRING DURING TOPICAL THERAPY WITH ASTEROL. (Journal American Medical Association, 150:1002, Nov. 8, 1952.)

From the observations of two cases, one in a boy of four years and another in a newborn female, the authors report that asterol, when applied topically, frequently is capable of causing encephalopathic toxicity consisting of generalized muscle tremors accompanied by disorientation and hallucinations. No other body functions seem affected. The symptoms may occur as early as the ninth day of therapy and may disappear in from three to six days following discontinuance of its use without apparent sequelae.

MICHAEL A. BRESCIA, M.D.

GRISWOLD, M. H.: CANCER OF THE PROSTATE IN INFANTS AND CHILDREN. (Journal American Medical Association, 150:791, Oct. 25, 1952.)

The author reports on two cases of malignancy of the prostate, one in a two-year-old and another in a six-year-old. The two-year-old was admitted to the hospital because of complete retention of urine. A month prior to admission the child complained of burning and frequency of urination. On examination the bladder was found to be palpable above the symphysis before evacuation and after evacuation there was still a large mass, about the size of an orange. Rectal examination revealed a round mass involving the prostate and extending upward above the examining finger. This mass was elastic. The tumor was removed and was determined to be a rhabdomyosarcoma grade-3 of the prostate with invasion of the blood vessels. The patient died and autopsy confirmed the diagnosis. The six-year-old boy complained of urinary disturbance, frequency and right sided backache for two days prior to hospitalization. The bladder was found to be distended up to the level of the umbilicus and the prostate was very firm and nodular. A punch biopsy of the prostate and inguinal lymph nodes was reported as anaplastic malignant tumor grade-3. The patient died with extensive metastasis, the final diagnosis being "possible neuroblastoma."

MICHAEL A. BRESCIA, M.D.

BACH, F.; FREEDMAN, A. AND BERNSTOCK, L.: RHEUMATIC FEVER. SOME OBSERVATIONS ON ACTH, CORTISONE AND SALICYLATE THERAPY. (British Medical Journal, 4784:582, Sept. 13, 1952.)

Four children severely ill with rheumatic fever and pericarditis showed a prompt improvement when treated with cortisone. The duration of treatment varied from 44 to 120 days. With reduction of dosage the signs and symptoms of rheumatic activity recurred. There was no increase of disability in the two patients who had previous rheumatic valvular disease. In the other two patients it was their first attack. One was left without apparent heart damage; the other appeared to be fully recovered, but shortly after relapsed following a throat infection. This patient responded to a course of ACTH, but a systolic murmur persists. In all of these cases some clinical features of adrenocortical excess were observed. Weekly examination of the serum cholesterol showed a constant rise during administration of either hormone. Four patients were then treated with high dosage of salicylates, and clinical and biochemical changes, similar to those in the hormone-treated cases, were noted. In particular, mention must be made of the development of red striae on the breasts of two girls, one treated with ACTH and the other with salicylates. The administration of salicylate was found to lead to an initial fall of the serum cholesterol followed by a rise which was maintained throughout the treatment. This initial fall resembles that seen when ACTH is given. It was concluded that it was justifiable to hold as a working hypothesis that salicylates exert their pharmacological activity by engendering adrenocortical excess. When salicylate, ACTH and cortisone are administered, rheumatic activity is suppressed.

AUTHORS' SUMMARY.

HAMMON, W. MCD.; CORIELL, L. L.; WEHRLE, P. F.; KLIMT, C. R. AND STOKES, J. JR.: EVALUATION OF RED CROSS GAMMA GLOBULIN AS A PROPHYLACTIC AGENT FOR POLIOMYELITIS. PRELIMINARY REPORT OF RESULTS BASED ON CLINICAL DIAGNOSIS. (Journal American Medical Association, 150:757, Oct. 25, 1952.)

In a series of three controlled field tests to evaluate the prophylactic effect of Red Cross gamma globulin in poliomyelitis, 54,772 children, between the ages of 1 and 11 years, were inoculated,

one-half of them with gamma globulin and one-half with a solution of gelatin. These three field tests were conducted in areas that were experiencing severe epidmics of poliomyelitis. The injections were given to apparently normal, healthy children living in the area, with the full understanding, permission, and cooperation of the parents. Which of the two materials any one child received was unknown to all—children, parents, and investigators—until completion of a follow-up period considered to be adequate for determining a final diagnosis. A preliminary tabulation of results, as of Oct. 1, 1952, shows that paralytic poliomyelitis had been diagnosed in 90 cases in the study groups. Analysis of these patients on the basis of the type of injection received shows that significant protection was conferred by the gamma globulin. During the first week after injection there was no significant reduction in the number of cases in the group receiving gamma globulin, but the severity of paralysis appeared to have been modified. From the second through the fifth weeks highly significant protection was demonstrated. After the fifth week this was less evident, but more definite conclusions regarding the duration of protection and possible modification of disease should be available after a longer period of follow-up. Laboratory studies, still incomplete, should give information regarding the effect of gamma globulin on in apparent infection and the subsequent development of active immunity.

AUTHORS' SUMMARY.

MATHES, S.; GOLD, H.; MARSH, R.; GREINER, T.; PALUMBO, F.; MESSELOFF, C. AND PEARLMUTTER, M.: COMPARISON OF THE TOLERANCE OF ADULTS AND CHILDREN TO DIGITOXIN. (Journal American Medical Association, 150:191, Sept. 20, 1952.)

Adults and children received digitoxin orally on the basis of body weight. Each patient received an average of three doses differing by 25 per cent. The effect that was measured was the percentage of patients showing a change in the RT-T segment of the electrocardiogram. The results are based on 217 doses given to 71 adults, 170 doses given to 54 children and the analysis of 2,322 Electrocardiograms. The results showed that, when the dose is calculated on the basis of body weight, children require about 50 per cent more digitoxin by oral administration than adults for the production of a similar effect. MICHAEL A. BRESCIA, M.D.

DURNIN, J. V. G. A. AND WEIR, J. R. de V.: STATURES OF A GROUP OF UNIVERSITY STUDENTS AND OF THEIR PARENTS. (British Medical Journal, 4766:1006, May 10, 1952).

The heights of 63 women and 184 men students at Glasgow University were compared with those of their parents. The mean height of the women students was 1.7 in. (4.3 cm.) more than that of their mothers, and the mean height of the men students was 1.8 in. (4.6 cm.) more than that of their fathers. It is difficult to believe, in accord with most present-day British authorities, that these differences are wholly due to shrinkage on the part of the parents, and the view is put forward that a real secular increase in height is at least a factor. AUTHORS' SUMMARY.

SMITH, A. B.: BRAIN TUMORS IN CHILDREN. (Radiology, 58:688, May 1952).

The author reports on 34 cases of brain tumor in children ranging in age from 11 months to 15 years. It is noted that one-sixth of all brain tumors occur in children under 15 years of age, two-thirds of them occurring beneath the tentorium, the majority of which are highly malignant. In 17 cases in which plain films of the skull were taken, 13 showed signs of increased intracranial pressure. Ventriculography was done in 16 patients. Dilated ventricles only were found in four, all with subtentorial tumors. Twenty-five of the 34 children were dead or unimproved at the end of a year and nine were living and improved for more than a year. The prognosis is worse in the younger age group, since medulloblastoma is more common in children of this age and they are poorer surgical risks. Under six years, 75 per cent of the tumors were subtentorial; over six years, the subtentorial tumors made up 60 per cent of the total number. MICHAEL A. BRESCIA, M.D.

TROWELL, H. C. AND DAVIES, J. N. P.: KWASHIORKOR. 1. NUTRITIONAL BACKGROUND, HISTORY, DISTRIBUTION AND INCIDENCE (British Medical Journal, 4788:796, Oct. 11, 1952). TROWELL, H. C.; DAVIES, J. N. P. AND DEAN, R. F. A.: 2. CLINICAL PICTURE, PATHOLOGY AND DIFFERENTIAL DIAGNOSIS. (Ibid, 4788:798, Oct. 11, 1952).

Kwashiorkor appears to be one of the major nutritional diseases.

It has been recognized by many African tribes, who have their own names for it. It is extremely common in the tropics and subtropics. It attacks children when their protein requirements are high. The disease has been described in Asia, Africa, tropical America and in the poorer towns of southern Europe. Although African children grow well while fully breast-fed, many of them fail to put on weight, develop brown hair and have attacks of diarrhea in the weaning and post-weaning periods. This is believed to be mild kwashiorkor. In the severe form, although edema is always present, the children are underweight and show retarded bone development. As a late manifestation, a unique dermatosis appears. The dermatosis has a different distribution from that of pellagra, but there may be superficial and histological resemblances. The hair usually becomes reddish or pale. Apathy and misery are constant features. Notable pathological lesions include the disappearance of zymogen granules from the pancreatic acini and the accumulation of fat in the periphery of the hepatic lobule.

MICHAEL A. BRESCIA, M.D.

BRODRIBB, H. S.; MCMURRY, J. AND SCOTT, L. G.: TWO CASES OF DIABETES MELLITUS IN INFANTS UNDER ONE YEAR. (British Medical Journal, 4767:1060, May 17, 1952).

Two further cases of diabetes mellitus, which began in infants under one year old, are described. The first had a gradual onset, which followed immunization, and was comparatively mild. The second was acute and severe, presenting pulmonary symptoms and signs; her blood sugar was 1,160 mg. per 100 ml., the highest recorded under the age of one year. Both patients survived, and continued well on two doses of soluble insulin daily.

AUTHORS' SUMMARY.

STICKNEY, J. M. AND MILLS, S. D.: CORTICOTROPIN AND CORTISONE IN BLOOD DISEASES IN CHILDREN. (Journal American Medical Association, 150:1278, Nov. 29, 1952).

Corticotropin and cortisone exert no significant effect on normal human bone marrow. These hormones, with the folic acid antagonists, constitute an addition to the therapeutic agents available for the treatment of acute leukemia. Remissions produced in 25 per

cent of children with acute lymphocytic leukemia in whom these hormones were used were spectacular, but such remissions are not long continued. Roentgen therapy or treatment with the nitrogen mustards is to be preferred to hormone therapy in the management of lymphoma. In acquired hemolytic anemia and thrombocytopenic purpura, benefit is seen after hormone therapy, but if the disease is severe, splenectomy is usually not avoided. Aplastic anemia does not respond to therapy with these hormones.

AUTHORS' SUMMARY.

KUMM, H. W.: RECENT ADDITIONS TO KNOWLEDGE OF POLIOMYELITIS. (Journal American Medical Association, 150:1179, Nov. 22, 1952).

During the past two years a number of significant advances have been made in the field of poliomyelitis but only a few are mentioned in this discussion. A report was published dealing with the first 100 strains of virus that have been classified into their broad antigenic groups. Three different immunogenic types were found. It was shown that second attacks of poliomyelitis may be caused by successive infections with different immunogenic types of virus. Viremia has been demonstrated during the incubation period of the experimental disease in cynomolgus monkeys and chimpanzees. It has been proved that in monkeys prophylactic injections of a blood fraction containing antibodies will prevent paralysis. The effects of such inoculations in human beings are now under investigation. Techniques have been developed for in vitro growth of virus in tissue cultures. The potentialities of this procedure for advancing the study of poliomyelitis are very great.

AUTHOR'S SUMMARY.

PHILPOTT, M. G.: THE SCHOENLEIN-HENOCH SYNDROME IN CHILDHOOD WITH PARTICULAR REFERENCE TO THE OCCURRENCE OF NEPHRITIS. (Archives of Disease in Childhood, 27:480, Oct. 1952).

Forty cases of the Schöenlein-Henoch syndrome in children have been analysed. Nineteen (47.5 per cent) developed nephritis; fourteen (35 per cent) suffered relapses and 12 of these developed nephritis. Of 11 patients developing nephritis, this is still active

in 4 after one year. Only 4 cases were encountered under the age of 2 years, including one infant of 8 months. Male cases were commoner than female in a ratio of 5:3. Throat infections preceded the disease in at least 55 per cent of the cases.

AUTHOR'S SUMMARY.

HALLMAN, N. AND TÄHKÄ, H.: OBSERVATIONS ON THE CEREBROSPINAL FLUID IN INFANTILE DIARRHEA. (Acta Paediatrica, 41:437, Sept. 1952).

1—A study of the cells in the spinal fluid, as well as Nonne and Pandy reactions, was made in 211 cases of infantile diarrhea of various degree of severity. 2—The number of cells in the cerebrospinal fluid was invariably (2-4 examinations) below 5 per cmm. in 100 cases, and it was found to be increased at least once as follows: 6-10 per cmm. in 30 cases, 11-20 per cmm. in 35 cases, 21-50 per cmm. in 29 cases, 51-100 per cmm. in 7 and over 100 per cmm. in 11 cases. The changes were generally more extensive in the severe cases, but the difference between them and the mildest cases, which did not exhibit any symptoms pertaining to the central nervous system, was not particularly significant. The majority of the cells were diagnosed as lymphocytes. 3—If the protein reactions are also taken into consideration, the spinal fluid was found within normal limits in only 13 patients. 4—The age at onset, the weight of the infant as compared with the expected weight, the alkali reserve on admission and other simultaneous infections do not seem to have any noteworthy effect on changes in the spinal fluid. 5—Changes were found to be more frequent in diarrhea produced by the Shigellas (35 cases) than in other cases due to an unknown causative agent. 6—Bacterial staining and culture of the cerebrospinal fluid were negative in all cases.

AUTHORS' SUMMARY.

BUNIM, J. J.; KUTTNER, A. G.; BALDWIN, J. S. AND MCEWEN, C.: CORTISONE AND CORTICOTROPIN IN RHEUMATIC FEVER AND JUVENILE RHEUMATOID ARTHRITIS. (Journal American Medical Association, 150:1273, Nov. 29, 1952).

Cortisone or corticotropin therapy produces prompt clinical improvement in the extracardiac manifestations of acute rheumatic

fever. The abnormal laboratory features are restored or tend to be restored to normal within a few weeks. The effects on the cardiac manifestations are more difficult to evaluate. Pericarditis subsides, as a rule, during the first week of therapy, although this may occur spontaneously. Congestive heart failure can be controlled provided salt intake is limited. Gallop rhythm frequently disappears, the heart sounds improve and the heart rate diminishes. Organic murmurs generally persist, even those of recent origin. Rheumatic activity persists in 50 per cent of the patients after the hormones are discontinued. At present it is not known whether the adrenal hormones result in the prevention or even significant diminution of damage to the heart. Adrenal cortical hormones suppress both the systemic and articular manifestations in almost all cases of juvenile rheumatoid arthritis. Relapses usually follow discontinuance of the hormones. MICHAEL A. BRESCIA, M.D.

NEUHAUSER, E. B. D.: WITTENBORG, M. H.; BERMAN, C. Z., AND COHEN, J.: Irradiation Effects of Roentgen Therapy on the Growing Spine. (Radiology, 59:637, Nov. 1952).

On re-studying 34 children who had received irradiation in which the spine was included in the field of therapy, growth disturbances were noted in the vertebrae which were directly related to dosage and inversely related to age. The significant changes on 11 post-mortem examinations were non-specific growth retardation and irregularity of ossification of the epiphyseal cartilage. Benign exostoses cartilagineae of the type commonly seen in multiple and familiar form appear to arise with greater frequency in bones whose epiphyses have been irradiated. The authors feel that when irradiation is definitely indicated in paravertebral tumors of the spine, x-ray therapy can be so directed as to produce minimal disturbances in development of the spine.

MICHAEL A. BRESCIA, M.D.

BOOK REVIEWS

SURVEY OF CLINICAL PEDIATRICS. By L. B. Slobody, M.D. Cloth. Pp. 471. Price $7.50. New York: McGraw-Hill Book Company, Inc., 1952.

Dr. Slobody has written a Survey of Clinical Pediatrics which should be of value, not only to medical students but also to general practitioners caring for children. The book is based upon the author's experience as a clinical teacher at the New York Medical College and The Metropolitan Hospital, in New York City. It is based upon manuals written for interns and residents on the pediatric service. Like many good books it has developed from daily use in the hands of students. It is in no way a substitute for the larger texts on pediatrics, but is rather a "desk-side" book which should be within easy reach of the physician and student, and as such, will be in constant use. Of special importance is the index. A book of this type is only as good as the index, and many books fail because of this deficiency. The reviewer has tried in vain to find an error in the index of Dr. Slobody's book. The great value of the book is its clearness and conciseness. No words are wasted, but all descriptions are accurate, readable and quickly available. No space is wasted on the very rare diseases, but sufficient description is given to make it possible for the student to classify them and investigate further if desired. The book has been brought up to the minute. It includes the use of the most recent antibiotics as well as the use of iso-nicotinic acid derivatives in tuberculosis. Each chapter concludes with a list of review questions which should be of great value to the student preparing for Board examinations. Dr. Slobody and his group of associates are to be congratulated upon the production of a book which should be of value to every pediatrician and general practitioner.

R. A. B.

CARBOHYDRATE METABOLISM. A SYMPOSIUM ON THE CLINICAL AND BIOCHEMICAL ASPECTS OF CARBOHYDRATE UTILIZATION IN HEALTH AND DISEASE. Edited by Victor A. Najjar. Cloth. Pp. 134. Price $4.00. Baltimore: The John Hopkins Press, 1952.

This small volume contains eight separate articles relating to carbohydrate metabolism. The purpose of this symposium is to

bring the laboratory information to the clinician as soon as possible and as Schwentker states in the preface, it is to have the laboratory scientist "present the newer knowledge on the subject and interpret it in such a way that it could be understood by those of us who are clinicians." The eight articles presented in the symposium are as follows: 1—The Enzymatic Synthesis and Molecular Configuration of Glycogen, by C. F. Cori. 2—Factors Affecting Liver and Muscle Phosphorylase, by E. W. Sutherland. 3—Studies on Glycogen Disease with Report of a Case in which Glycogen was Abnormal, by D. H. Andersen. 4—Pituitary Inhibition of Glucose Uptake by the Muscle, by C. R. Park. 5—Factors Affecting the Metabolism of Glucose and Pyruvate in vitro, by A. B. Hastings. 6—Spontaneous Hypoglycemia: Clinical and Metabolic Studies, by I. McQuarrie. 7—Some Observations on the Interrelationship of Potassium Metabolism and Carbohydrate Metabolism in the Isolated Rat's Diaphragm, by E. Calkins and I. M. Taylor. 8—The Therapeutic Implications of Disturbances in Water and Electrolyte Metabolism in Diabetic Acidosis.

MICHAEL A. BRESCIA, M.D.

MANAGEMENT OF THE NEWBORN. By Arthur H. Parmelee, M.D. Cloth. Illustrated. Pp. 358. Price $7.00. Chicago: The Year Book Publishers, Inc., 1952.

Although there is no pretense to offer this book as a textbook, nevertheless it contains so much valuable information and down to earth good sense that this small volume becomes a must to read. The book is written and read with ease, one getting the impression that an experienced clinician with teaching ability is imparting knowledge gained from long experience, albeit without consciously doing so. The chapters on "Characteristics of the Newborn" and "Disturbances Due to Abnormal Variations of Physiologic Peculiarities" are especially valuable and informative. The book is highly recommended. MICHAEL A. BRESCIA, M.D.